Supreme Court, U.S.
FILED
MAY 23

No. 01-1188

In The
Supreme Court of the United States

BALDEV RAJ BHUTANI and
ALRA LABORATORIES, INC.
Petitioners,

v.

UNITED STATES OF AMERICA,
Respondent.

ON PETITION FOR WRIT OF CERTIORARI
TO THE UNITED STATES COURT OF APPEALS
FOR THE SEVENTH CIRCUIT

REPLY BRIEF OF PETITIONERS

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REPLY BRIEF FOR PETITIONERS

I. THE GOVERNMENT DOES NOT DISPUTE THE MERITS OF THE NINTH CIRCUIT'S HOLDING IN *UNITED STATES V. WATKINS*.

Defendant Raj Bhutani has been sentenced to 30 months in prison for committing violations of the FD&C Act with "intent to defraud or mislead." The jury was not instructed that it had to find the violations were material. Three years after the jury's verdicts, this Court held that when Congress used the common law term "to defraud" in the mail and wire fraud statutes, it necessarily incorporated materiality as an element of the offense. *United States v. Neder*, 527 U.S. 1 (1999).

On January 29, 2002, the Ninth Circuit held that this Court's *Neder* opinion required a finding that materiality was an element of an "intent to defraud or mislead" under the felony provisions of the FD&C Act. *United States v. Watkins*, 278 F.3d 961 (9th Cir. 2002). The United States did not seek review of the *Watkins* panel opinion, and the Brief for the United States in Opposition in this case ("Opposition") does not argue that *Watkins* is wrong, or that *Neder*'s reasoning does not apply to the FD&C Act's felony provisions. Instead, the government argues that Defendants' request for a materiality instruction was incomplete, that the evidence proved that the offenses were material, and that the Seventh Circuit's failure to specifically address the fully-briefed materiality issue means that there is no published conflict between the Seventh Circuit's opinion here and the Ninth Circuit's opinion in *Watkins*. Opposition at 5-10.

This Court does not have to reach government arguments that the Seventh Circuit did not address. If the government does not dispute that materiality is an element of the FD&C Act's felony provisions, this Court should remand to the Seventh Circuit for reconsideration in light of *Watkins*, or

resolve the conflict between *Watkins* and the Seventh Circuit's ruling in this case.

Defendants did request a materiality instruction. Counsel told the district judge, "I want to preserve our objection to your failure to grant Alra request No. 12, which is the request for a materiality requirement on the failure to maintain records charges on that prong of the conspiracy count." Tr. 5863. The district judge responded, "In regard to the point about the failure to maintain records, my view on that, as I stated earlier this morning off the record, is that the regulations required the maintenance of these records and that establishes the need to keep them and to ask the jury to go beyond that and determine whether the records required to be kept by a federal regulation were material or not would be to give the jury the authority to modify the regulations, which I don't think would be a good idea." Tr. 5868.

The Indictment alleged that Defendants conspired to commit the object offense of a failure to maintain required records. Count One, paragraph 10(b)(J.A. 73). Accordingly, a request to define that object offense in the conspiracy count applied to all counts alleging a violation of Current Good Manufacturing Practice ("CGMP"), which includes a requirement of maintaining accurate records. *See* Count One, paragraph 9; Count Three; Count Six; Count Ten (J.A. 71, 87, 91, 99). The district judge refused a defense request to define how Defendants were alleged to violate CGMP on Count Ten, meaning that the jury may have convicted on Count Ten based on a record-keeping theory. Tr. 5867. The district judge's rationale for denying the requested materiality instruction applied to all counts alleging a failure to maintain records. The failure to give a materiality instruction on all FD&C counts was also plain error. *See Johnson v. United States*, 520 U.S. 461, 468 (1997)(error measured by established law at time of appeal).

The government argues that on Count Four alone, the jury was instructed that it had to find the Defendants "materially altered the manufacturing procedures." Opposition at 6. First, the district judge did not give a similar instruction on Counts One, Three, Six, and Ten. Second, there is a distinction between materially altering a "manufacturing procedure," and maintaining batch records. The district judge refused to tell the jury that any inaccuracies in the records had to be material, clearly believing that was not the law, and reflecting his belief that the instructions as a whole did not tell the jury that such a requirement existed. And third, Count Four did not charge a crime. *See* section II. below.

The government's description of the facts in support of its plain error analysis is inaccurate and incomplete. The district judge who presided over the trial wrote, "It seemed to the court at the time that the verdict could have gone either way . . . ." App. 64. On Counts Three, Four, and Six, where the government alleged that adding sodium hydroxide was a violation of the FD&C Act, Defendants did contend that the conduct did not happen, but also noted that the FDA had approved adding sodium hydroxide to the product. Defendants testified that adding sodium hydroxide was just repeating a step in the FDA-approved manufacturing process, and that FDA did not consider repeating a step in an approved manufacturing process to be a violation of CGMP. Tr. 5153-56, 5402, 5408-09. There was no evidence that the Bhutanis directed employees to falsify batch records; to the contrary, a mid-level supervisor who did not speak good English told employees what to write on the batch records to describe the reprocessing operation. Tr. 1740-41, 4407-11.

The government argues that testimony from defense expert Dr. Robyt that improperly mixed sodium hydroxide would have burned the mouths of patients demonstrated that the addition of sodium hydroxide was material.

Opposition at 8. The government has this argument backwards. There were no complaints of any burning sensations from customers, demonstrating that it was highly improbable that more sodium hydroxide was added at all, and conclusively proving that if sodium hydroxide was added, it was mixed sufficiently. With the government changing its position on appeal and conceding that the product was medically effective and stable, and in the absence of consumer complaints, the government's evidence failed to prove an intent to defraud with respect to a material matter. As the district court said at sentencing:

> Taking the counts one by one, there is no evidence that Dr. Bhutani regarded the injection of Lactulose into the individual bottles with syringes as creating a risk of serious bodily harm to people who might use the Lactulose Syrup. What was being injected was sodium hydroxide, which was something that was normally added to the drug. What occurred here was that it was added in a different manner than authorized by regulations, and the addition in that manner was not documented. . . .
>
> The government had itself changed its position as to what the risk was at least three times during the course of this litigation. It told the jury at trial that the risk was in the Lactulose itself in that it had degraded or decomposed to the point where it was no longer medically effective and that the injections of the sodium hydroxide were made to mask or conceal that fact. . . .
>
> When the case went up on appeal, the government took a different position . . . .

Tr. 1/24/00 at 39-41.

For the reasons stated in Section IV below, unrebutted defense expert testimony demonstrated that the use of lactulose raw material that arrived in leaking drums (Counts Seven and Eight) did not create a reasonable possibility of contamination. Perhaps most damning to the government's case on materiality, FDA inspector Stojak arrived at Alra's plant within weeks after the leaking drums were used, and heard directly from Dr. Bhutani that Alra had used material from leaking drums. Stojak did not even write up the use of the drums as a violation of the FD&C Act on his inspection report, and took no steps to recall the batch or initiate any enforcement action. Tr. 4028-4052.

As the district court said at sentencing: "there is no evidence whatever that the Lactulose that was used from the leaking drums had anything medically dangerous about it or that it would cause anybody any injury." Tr. 1/24/00 at 39-41.

The Opposition summarizes the evidence on Count Ten by saying, a Asteel pipe was dropped into a blender and ground up into the product, "and that such an event would be "obviously material." Opposition at 9 (emphasis added). First, such an event would be "obviously" impossible; a steel pipe hitting a moving grinder blade would stop the machinery. There was no evidence that a steel pipe was "ground up." Romiro Gonzalez, an ex-Alra employee with no motive to lie, testified that his brother Bernabe had let the pipe slip into a Fitzmill, and showed him the mangled pipe afterward. Romiro took the pipe to Dr. Bhutani, who told him to throw away the barrel of product that had been under the grinder at the time of the accident. Tr. 5179-81. Tr. 5179-81. Eleanor Campbell and Dr. Bhutani said the same thing. Tr. 2699, 5281-82. Carol Hacker, one of the government's key witnesses, had recorded the destruction of a drum of K+10. Tr. 1342-43 (J.A. 538). Hacker testified that Dr. Bhutani told her to use magnets to search for metal, and that she removed all the metal she could see. Tr. 1346.

Joyce Meton, a key government witness, testified that the magnets were picking up the metal. Tr. 1779. FDA District Director Raymond Mlecko testified that, at a meeting with Dr. Bhutani in 1991, FDA representatives did not disagree that the use of magnets to search for metal contamination was common in the industry. Tr. 3914. FDA did exhaustive lab testing on Alra's products looking for metal, and found none. Tr. 3211.

The failure to give a materiality instruction seriously affected petitioners' substantial rights and the fairness, integrity, and public reputation of judicial proceedings in this case.

II. THERE IS NO AMBIGUITY IN THE PLAIN LANGUAGE OF SECTION 331(e); COUNT FOUR AND AN OBJECT OF THE CONSPIRACY DID NOT ALLEGE A CRIME.

At the time of the conduct alleged in Count Four of the Indictment, the charged statute, 21 U.S.C. 331(e), provided that "the failure to establish or maintain any record . . . required under [21 U.S.C. 355(j)]" was a violation of the FD&C Act. 21 U.S.C. 355(j) did not include record-keeping requirements. The government's Opposition says that the Seventh Circuit's opinion upholding the convictions on Count Four "gave continuing meaning" to 331(e)'s reference to "establish[ing] or maintain[ing]" records. Opposition at 12. But the Seventh Circuit's opinion did not suggest there was any ambiguity in the statutory language. As the Seventh Circuit recognized, "the plain language of the statute did not penalize [Defendants'] conduct." App. 6.

The government does not dispute that this issue is a fundamental question of democratic theory, or that requiring Congress to specify criminal conduct is a restraint on the power of the prosecution to create crimes through interpretations of legislative intent. Further, the government's Opposition fails to address the crucial point

that section 331(e) was one of the object offenses alleged in the conspiracy charged in Count One. (J.A. 73).

III. THIS COURT SHOULD CORRECT THE SEVENTH CIRCUIT'S ERRONEOUS HOLDING THAT "JUDGES MUST APPLY THE GUIDELINES IN FORCE WHEN A DEFENDANT IS SENTENCED," AND REMAND.

The government's Opposition does not dispute that the Seventh Circuit's rejection of an ex post facto argument with the holding that "judges must apply the guidelines in force when a defendant is sentenced" is an incorrect statement of law that conflicts with all other federal circuits that have considered the issue. App. 11; Opposition at 14. Instead, the government argues "no harm, no foul," because the commentary to U.S.S.G. 2N2.1 at the time of the charged conduct provided that "[i]f the offense involved . . . fraud, . . . apply the guideline applicable to the underlying conduct." Defendants have substantial arguments that the underlying conduct here does not involve a 2F1.1 fraud. Guideline 2N2.1 has always applied to knowing conduct that violates the Food, Drug & Cosmetic Act. Application Note 1 provides, "This guideline assumes a regulatory offense that involved knowing or reckless conduct." Cases like this one, alleging an intent to defraud FDA, where the jury is instructed that "[i]t is not necessary . . . that the defendant intended to cause economic loss," J.A. 497, fit that category. At most, the government's evidence showed knowing, technical violations of the FD&C Act. This Court should correct the Seventh Circuit's error of law and remand for reconsideration of Defendants' sentencing arguments.

IV. THE GOVERNMENT DOES NOT ADDRESS THE LEGAL EFFECT OF UNREBUTTED EXPERT TESTIMONY DENYING AN OFFENSE ELEMENT.

The government's Opposition does not address the legal basis for certiorari, that the Seventh Circuit's opinion

conflicts with precedent from other circuits finding that unrebutted defense expert testimony denying an element of the offense rendered the government's evidence insufficient as a matter of law. Instead, the government argues that Dr. Robyt's testimony was based on incomplete information. That is not true. For a complete summary of the essentially undisputed facts on Counts Seven and Eight, *see* Petitioners' brief to the Seventh Circuit at 28-36, 43-48.

The government repeatedly refers to an allegation that Dr. Bhutani instructed employees to inject glue into the leaks in the drums. That allegation came solely from the uncorroborated testimony of James Ward, who was fired for incompetence and committed repeated, demonstrable perjury. No one saw any glue on the drums, photographs of the drums did not show any glue, and FDA inspector Stojak testified that during September 1989, he saw drums with tape, but did not see any glue, even though he was looking for it. Tr. 2206-20, 2277, 4023-24. For a catalogue of Ward's demonstrated, extensive lies, *see* Petitioners' brief to the Seventh Circuit at 28-36, 43-48. Dr. Bhutani's preliminary opinion that the drums could not be used came before Alra's Quality Control lab tested each drum and found no contamination.

V. THE GOVERNMENT IGNORES THE SEVENTH CIRCUIT'S HOLDING THAT VIOLATIONS OF A REGULATORY SCHEME, NOT "THE MEDICAL [IN]EFFECTIVENESS OF THE DRUG," ARE SUFFICIENT TO PROVE A "FRAUD LOSS."

The government's Opposition argues that the Seventh Circuit's opinion is consistent with *United States v. Marcus*, 82 F.3d 606 (4th Cir. 1996), because this case "implicates the safety and efficacy of the [Defendants'] product[s]." Opposition at 16-17. That is not what the district court or the Seventh Circuit said. The district court found that there was "no evidence of any actual contamination" (1/24/00

hearing at 40-41), that this "was a paper case" about "failure to keep records," that there was "no showing of any harm to anybody" (2/15/00 hearing at 124), and that there was "no evidence that anyone was likely to be hurt from these tiny metal fragments that were in some of the pills" (1/24/00 hearing at 41). In conflict with *Marcus* and many other cases, the Seventh Circuit panel rejected the idea that safety and efficacy of the products controlled. The panel wrote: "[t]he medical effectiveness of the drug or its dangerousness after adulteration ought not to be the core of the inquiry; . . . there was indeed loss to consumers because consumers bought drugs under the false belief that they were in full compliance with the law." App. 13.

If the Sentencing Commission ever resolves the conflict between the Seventh Circuit's opinion here and *United States v. Maurello*, 76 F.3d 1304, 1312 (3d Cir. 1996); *United States v. Chatterji*, 46 F.3d 1336 (4th Cir. 1995); *United States v. Haas*,171 F.3d 259, 269-70 (5th Cir. 1999); *United States v. Barnes*, 125 F.3d 1287 (9th Cir. 1997); *United States v. Haddock*, 12 F.3d 950, 960-61 (10th Cir.1993); and *United States v. Prigmore*, 1996 U.S.Dist. Lexis 11695 (D.Mass. 1996), it will be cold comfort to Dr. Bhutani while he serves 30 months in prison.

VI. THE GOVERNMENT REFUSES TO CORRECT ITS MISREPRESENTATIONS TO THE SEVENTH CIRCUIT.

The government asked the jury to convict Defendants on Counts Three and Six on the grounds that the Lactulose from lots 52-230 and 52-231 "had decomposed so that it no longer met applicable testing specifications." (Jury instructions, J.A. 501). Government counsel told the district court three days before trial that "the government's theory of the case" was that the Lactulose Syrup was "no longer stable" before the sodium hydroxide was added. Tr. 12/4/95 at 5. Government counsel told the district judge during Rule 29 argument that the evidence presented to the

jury proved that Alra's Lactulose was medically ineffective before the alleged addition of sodium hydroxide. Tr. 4232-3. Government counsel told the jury during closing argument that "Lactulose is an unstable sugar." Tr. 5612 (emphasis added).

In its brief to the Seventh Circuit, the government said it told the jury exactly the opposite of what it told the district judge, and exactly the opposite of its theory of conviction on Counts Three and Six: "the government represented to the jury that the Lactulose in question was at all times within approved specifications." Govt. Br. at 15. The district court knows that the government changed its position on appeal. App. 19. Petitioners' counsel has repeatedly asked the Department of Justice to correct its misrepresentations to appellate courts in this litigation. *See* letters from Petitioners' counsel to Department of Justice, attached to this reply.

The Opposition's refusal to correct the record is one more act in an ongoing judicial scandal.

CONCLUSION

The petition for a writ of certiorari should be granted.

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Re: United States v. Bhutani, et al.

Dear Counsel:

Defendants feel that they are witnesses to a judicial scandal, but no one is listening. The government told the Seventh Circuit things that were not true, and the Seventh Circuit relied on those factual errors in its opinion. Defendants have filed a petition for certiorari, but the Supreme Court takes only 100 cases a year. Unless someone inside the Department of Justice takes the time to understand the details of this case, and to understand why the government's representations to the Seventh Circuit were wrong, a grave injustice will occur.

FACTUAL BACKGROUND

After a ten-week trial, the jury convicted Dr. Baldev Raj Bhutani, his wife Neelam Bhutani, and Alra Laboratories, Incorporated ("Alra") of conspiracy and various violations of the Federal Food, Drug and Cosmetic Act ("FD&C Act"). The Bhutanis own and run Alra, a generic drug manufacturer.

The lead allegations in the Indictment, which were the primary focus at trial, related to Alra's manufacture of lots 52-230-P and 52-231-P of Lactulose Syrup, USP. Lactulose Syrup is a prescription laxative, produced in liquid form, that treats liver disease by removing ammonia that builds up in the colon. Tr. 1575, 1691-97.

Alra first mixed the bulk solutions for lots 52-230 and 52-231 in June, 1986, and bottled the lots. After getting approval to market Lactulose Syrup from the Food and Drug Administration (AFDAA) in July, 1988, Alra's Quality Control laboratory tested samples from both lots. Each lot assayed at 100% of label claim for the active ingredient, and the pH values for the two lots ranged from 5.3 - 5.6, well within the approved pH range for Lactulose Syrup of 3.0 - 7.0. Lab tests for related substances, which are measurements of saccharides that would be present if the active ingredient was breaking down, were also well within limits. Joint Appendix in the Seventh Circuit ("J.A.") at 377, 398.

The Government contended that despite these passing lab results, Defendants nonetheless believed that the lots were "degraded" and "decomposed," and that to mask that decomposition, seven Alra employees unpacked both lots from storage crates, opened each of approximately 3,300 bottles from the two lots, added sodium hydroxide (an ingredient in Alra's FDA-approved formulation) bottle-by-bottle with some

sort of turkey baster or syringe, shook the bottles, recapped the bottles, labeled them, and repacked them in crates. The Government alleged that this process violated the FD&C Act because Alra's approved manufacturing process required that sodium hydroxide be added in a mixing vat during the initial manufacture of Lactulose Syrup. The Government also charged that Alra created false batch records because the employees failed to document the alleged addition of sodium hydroxide. J.A. 65-66, 69-70. The defense acknowledged that seven employees had unpacked the bottles, replaced some leaking caps, labeled the bottles, and repacked them, but the defense denied that additional sodium hydroxide had been added as alleged in the Indictment.

Defendants were convicted of conspiracy and various substantive counts.

In May, 1996, three months after the jury's verdict, the United States Pharmacopeia ("USP") proposed a downward revision of the acceptable pH range for Lactulose, from 3.0 - 7.0 to 2.5 - 6.5. The USP based its proposal on data submitted by UDL, another manufacturer of Lactulose. The USP proposal stated:

> [b]ased on information received that stability data has shown a downward trend in pH over time, it is proposed to revise the pH range in this monograph. The proposed pH change is reported not to have any significant impact on the safety and quality of this product: it does not in any way affect the laxative properties of the product, and it does not affect the level of the related substances.

J.A. 284-85.

The defense filed a Motion for a New Trial Based on Newly Discovered Evidence And/Or Violation of Brady v. Maryland, arguing that the data cited by the USP was in the possession of FDA before the trial and undercut the Government's theory that a decline in pH correlated to a decline in medical effectiveness. J.A. 269-85. The defense followed up with a motion for discovery, requesting the stability data from other manufacturers of Lactulose in FDA's files. J.A. 292. The district court ordered discovery over the Government's opposition. J.A. 301.

The data from other manufacturers that was in FDA's files before trial showed that there was no correlation between a decline in pH and the potency of the product; showed that Lactulose was stable as a rock, plateauing at over 90% of label claim for years after manufacture even as pH declined to 3.0 and below; and showed that there was no "cascading" effect or accelerated degradation of the product at pH values of 3 or below. See Memorandum in Support of Post-Trial Motion, filed May 12, 1997; J.A. 343-51. Discovery revealed that on August 15, 1994, UDL had submitted its stability data to FDA showing no correlation between a decline in pH and the potency of the product, and had asked FDA to revise the pH range downward. A year later the Government argued a scientific theory to the jury directly contrary to the UDL data.

Data in FDA's files before the trial exposed the Government's theory of motive as fiction. Government counsel had argued that Alra wanted to increase the pH of the Lactulose lots to "make sure that if anyone tested the pH of the drug product, it would test high. They wouldn't know it was old, they wouldn't know it had degraded." Tr. 5585. Alra was the first generic manufacturer of Lactulose approved by the FDA. And lots 52-230 and 52-231 were among the first five lots that Alra released. The other three lots that Alra released at roughly the same time had pH values ranging between 4.9 and 5.85 at

the time of release. Alra's customers thus would not have known anything about the age of lots 52-230 and 52-231 from comparing their pH values to other Alra lots.

Post-trial Brady discovery revealed that Merrill Dow, the name brand manufacturer that had monopolized the market for Lactulose in the U.S. for years, generally released product with initial pH values between 4.0 and 5.0. According to the Government's theory that a higher pH value would indicate a "newer" product, any sophisticated customers familiar with Lactulose would have believed that any product with a pH above 4.5 was "new." There was thus no motive at all for Alra to increase the pH of its lots.

The Government did not call any Alra customers at trial to testify that they would have believed that a product with a pH of 4.6 was "old." In light of the revelation that the innovator routinely released product with pH values between 4.0 - 5.0, defense counsel doubt that the government even asked any Alra customers whether they would have recognized the "age" of any batches based on pH values well within specifications. It appears that the Government constructed this theory based on speculation, without ever checking the contrary evidence in FDA's files.

The district court requested extensive briefing from the parties summarizing the stability data that had been in FDA's possession before trial, and on the government's use of the word "degradation" during trial. Finally, in a 30-page Memorandum Opinion that quoted extensively from the government's arguments to the jury and its questions to expert witnesses, the district court found that the government had suppressed the stability data in FDA's files, that the data was favorable to the defense, and that the data was material. Explicitly finding that the stability data in FDA's files "seriously undermines the court's confidence in the verdicts,"

the district court granted Defendants' motion for a new trial. Memorandum Opinion, 12/17/97, Appendix B to Petition for Cert.

The government appealed. On appeal, the National Pharmaceutical Alliance "(NPA"), a national trade association representing more than 160 generic pharmaceutical manufacturers, distributors, and related firms, was granted leave to file a brief amicus curiae. The NPA was concerned about the government's argument that the prosecution team had no obligation to search FDA's files for exculpatory materials in an FD&C Act prosecution. The NPA argued that because of the FDA's "special place in our health care system:"

> [i]t is absolutely necessary that the FDA be obligated to take enforcement action only when-as an agency-it can assure the Court that its position is fully supported by the data and information in its files. To suggest that it may proceed in a civil or criminal matter without conducting a thorough review of its own files is absolutely contrary to the responsibility that Congress has placed on the agency.

Brief Amicus Curiae of the National Pharmaceutical Alliance in Support of Affirmance, at 2.

I. THE SEVENTH CIRCUIT'S OPINION ADOPTED THE GOVERNMENT'S MISRERESENTATIONS ABOUT THE PROSECUTION'S ARGUMENTS AT TRIAL.

In briefing, the government told the Seventh Circuit that it "did not dispute that before being spiked with sodium hydroxide [lots 52-230 and 52-231] were within the pH range, medically effective, and stable." Reply Brief of Appellant at 6.

Government counsel repeated that position during oral argument, saying:

> we never argued the material was decomposed due to its aging. The only decomposition which comes into matter from the evidence produced at trial was once they added the sodium hydroxide to it that then sent a chain of events into causation here including the acceleration of the degradation of the drug so it's possible that after they added the sodium hydroxide then it at least in part was a decomposed product.

During oral argument on appeal, the government said that it had argued that the Lactulose was dangerous only after the alleged addition of sodium hydroxide:

> That's true we so argued [that the product was dangerous] but what Judge Grady said is that we argued that they spiked it because it was dangerous before they spiked it. There's a big difference from saying it was dangerous after they spiked it which the defense expert Robyt testified as well, that if by spiking the bottle by bottle with sodium hydroxide that would be greatly dangerous there was no dispute on that as well. So that evidence in testimony about after spiking it being dangerous simply does not support the district court, the district court's holding here.[1]

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[1] Transcription from tape of oral argument.

The Seventh Circuit adopted the government's argument, writing, After reviewing the trial transcript, we do not agree that the government's argument was premised on the fact that ALRA spiked the Lactulose lots because they would soon be unfit for use. In fact, the government did not argue that the Lactulose was unfit, or close to unfit." 175 F.3d at 578.

II. THE GOVERNMENT CONTENDED THAT THE LACTULOSE WAS MEDICALLY INEFFECTIVE, UNSTABLE, AND "CLOSE TO UNFIT" THROUGH INDICTMENT, TRIAL, AND SENTENCING SUBMISSIONS.

A. That The Lactulose Was "Decomposed" And Unfit Before The Alleged Addition Of Sodium Hydroxide.

On January 12, 1994, FDA Inspector Joseph Stojak summarized to the grand jury the evidence supporting the government's proposed superseding indictment. He testified:

> They went back-when they tested the product, they found that the pH, an indicator of the stability of the product, had dropped significantly. They went back in, opened up each of the caps and actually syringed in additional sodium hydroxide into the container, closed the caps, and shook them up.
>
> What they were trying to do and what they ultimately convinced themselves they did was that they raised the pH, and therefore, the product was good again.

Q. When you say that the increase of pH and the injection of sodium hydroxide would mask the degradation of the product-is that right?

A. -Exactly, the pH-

Q. -It was not actually restored, in fact, to its previous position?[2]

A. No, it wasn't restored at all, but it would mask this by, if anyone were to check the product, they would say the pH is within range; therefore the product must be good.

. . .

Q. What happened after the injection of sodium hydroxide into the finished lots-were the bottles then relabeled?

A. Yes, they were relabeled, and this is a very odd situation. They relabeled them-keep in mind they were made in '86 and they're allowed to have an eighteen-month expiration, and here we're all the way into '88-they relabeled these products with a September of 1989 expiration date.

Q. So the product had in fact already expired; is that right?

A. It had long expired.[2]

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[2] Grand jury testimony of Joseph Stojak, 1/12/94, at pp. 20-21 (emphases added).

Agent Stojak clearly told the grand jury that Lactulose lots 52-230 and 52-231 were no good before the alleged addition of sodium hydroxide. He testified that the lots had "expired." According to the government's position before the Seventh Circuit, Inspector Stojak really said:

> They went back-when they tested the product, they found that the pH, [which is not an indicator of the medical effectiveness of the product], had dropped [in a way that did not affect the stability or medical effectiveness of the product]. They went back in, opened up each of the caps and actually syringed in additional sodium hydroxide into the container, closed the caps, and shook them up.
>
> What they were trying to do and what they ultimately convinced themselves they did was that they raised the pH, and therefore, the product [that had been safe, medically effective, and stable, was now dangerous].
>
> Q. When you say that the increase of pH and the injection of sodium hydroxide would mask the degradation of the product [that was safe, medically effective and stable]-is that right?
>
> A. -Exactly, the pH-
>
> Q. -It was not actually restored, in fact, to its previous position [of being medically effective and stable]?[3]

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[3] Grand jury testimony of Joseph Stojak, 1/12/94, at pp. 20-21 (emphases added).

A. No, it wasn't restored at all [the Defendants had changed the product from being safe, medically effective and stable to being dangerous, and the new pH level which had caused this dangerous condition], would mask this by, if anyone were to check the product, they would say the pH is within range; therefore the product must be good.

. . .

Q. What happened after the injection of sodium hydroxide into the finished lots-were the bottles then relabeled?

A. Yes, they were relabeled, and this is a very odd situation. They relabeled them-keep in mind they were made in '86 and they're allowed to have an eighteen-month expiration, and here we're all the way into '88-they relabeled these products with a September of 1989 expiration date.

Q. So the product had in fact already expired [but was still safe, medically effective, and stable]; is that right?

A. It had long [been safe, medically effective, and stable, and would have been stable and medically effective for years if Defendants hadn't added the sodium hydroxide].

B. The Indictment Alleged That The Lactulose Was "Decomposed" Before The Alleged Addition of Sodium Hydroxide.

Overt Act 2 in the conspiracy count alleged: "BALDEV RAJ BHUTANI and NEELAM BHUTANI directed ALRA employees to add an undocumented substance, namely additional amounts of Sodium Hydroxide (NaOH), to partially decomposed Lactulose in the finished generic drug product Lactulose Syrup, USP. . . ." (Emphasis added).

Overt Act 5 in the conspiracy count alleged: "BALDEV RAJ BHUTANI and NEELAM BHUTANI caused the shipment from Gurnee, Illinois to Brooklyn, New York, of an adulterated ALRA generic drug product, Lactulose Syrup, USP, lot number 52-230-P, which contained a decomposed substance, namely decomposed Lactulose, and an undocumented and unapproved substance, namely additional amounts of Sodium Hydroxide (NaOH)." Counts 3 and 6 of the Superseding Indictment also alleged that lots 52-230 and 52-231 "consisted in part of a decomposed substance, namely decomposed lactulose raw material."

Overt Act 2 did not allege that the Lactulose became decomposed after the addition of sodium hydroxide. Instead, it alleged that Defendants added sodium hydroxide to "partially decomposed Lactulose."

The Indictment provides conclusive proof that the Government alleged that the Lactulose was not medically effective, stable, fit, or close to fit. According to the government's current theory of its allegations, the Indictment should have read: "BALDEV RAJ BHUTANI and NEELAM BHUTANI directed ALRA employees to add an undocumented substance, namely additional amounts of Sodium Hydroxide

(NaOH), to [medically effective, stable, and fit] Lactulose in the finished generic drug product Lactulose Syrup, USP . . . ."

C. The Government's Expert Witness Disclosure Emphasized That pH Was Evidence of "Degradation."

Before trial, the government filed an expert witness disclosure. That disclosure said that Kevin Hicks, Ph.D., would testify that "degradation of Lactulose can be evidenced by a reduction in the solution's pH. Raising of the pH through the addition of NaOH may mask the detection of the degradation of Lactulose, but it would not reverse the degradation process." Expert Witness Disclosure at p. 2. The Expert Witness Disclosure said that the addition of sodium hydroxide would "mask" degradation that had already occurred.

Acording to the government's theory in front of the Seventh Circuit, the Expert Disclosure really meant: "[insignificant] degradation of Lactulose can be evidenced by a reduction in the solution's pH [that would not indicate that the product was unsafe, unstable, or medically ineffective]. Raising of the pH through the addition of NaOH may mask the detection of the [insignificant] degradation of Lactulose, but [would cause the product to be unsafe and medically ineffective and unstable]."

D. At A Hearing One Month Before Trial, The Government Stated That It Would Call An Expert To Testify That The Product Had Decomposed Due To Its Age.

At a hearing on November 8, 1995, one month before trial, the Court asked government counsel what kind of expert testimony it would present. Government counsel said:

> Your Honor, we will have a chemist who will describe what Lactulose, Lactulose being one of the drugs in question, is, basically what happens to it after time, the charge being that it was sold after its expiration date; so from the standpoint of an expert in carbohydrates and sugar chemistry will describe what in fact it was several years after manufacture.
>
> . . .
>
> . . . That will be followed by a gastroenterologist who will be from the FDA Center for Drug Evaluation Research, specifically a fellow by the name of Dr. John Senior who will testify as to why with those changes it would not have the same therapeutic effect from the standpoint of a gastroenterologist.

Tr. 11/8/95 at 11 (emphasis added). Government counsel was not discussing "changes" from the alleged injection of sodium hydroxide; counsel was discussing "changes" as a result of the aging of the product. The government told the Seventh Circuit, "we never argued the material was decomposed due to its aging."

E. Three Days Before Trial, The Government Argued To The District Court That Lactulose Lots 52-230 and 52-231 Were "No Longer Stable."

On December 5, 1995, three days before trial, government counsel told this Court at a hearing that "it is the government's theory of the case-after but prior to the manufacture, three years and stuck in storage, it then was approved. It was approved in an 18-month [expiration] date

based on stability data that was submitted. Then after 18 months, it was no longer stable. It no longer could be assured that it is what it originally was." Tr. of 12/5/95 hearing at 5.

F. In Opening Statement The Government Argued That The Lactulose Was Not Stable.

Contrary to its representations to the Seventh Circuit that it "did not dispute that [lots 52-230 and 52-231] were . . . medically effective and stable" before the alleged addition of sodium hydroxide, government counsel argued in opening statement that the lots had "expired," and that attempting to market them was doing the "wrong thing:"

> But then the Bhutanis chose to do the wrong thing. Alra received its ANDA approval to sell Lactulose in August of 1988. Now, that was a full two years after the initial 1986 batches were manufactured. The government will show you that on the week that Alra's ANDA for Lactulose was approved, the defendants Baldev Raj Bhutani and Neelam Bhutani instructed their employees to label the bottles of Lactulose that had been manufactured in 1986 with a September 1989 expiration date.
>
> Now, that date was over three years from the date the product was actually manufactured, well beyond the 18-month approved and accepted expiration date. And then they took that mislabeled expired product and they shipped it out the door.

Tr. 12/8/95 at 15-16 (emphases added). The government told the jury that the product was "expired" because of its age. The

government told the Seventh Circuit that "we never argued the material was decomposed due to its aging."

G. The Government Stated Its Theory That A Decline In pH Showed "Degradation" In Its Opening Statement.

In her opening statement, Government counsel argued:

> The defendants instructed their employees to open up the bottles of Lactulose, those 1986 bottles, and inject a chemical called sodium hydroxide into the bottles in order to raise the pH and make it appear that the product had not, in fact, degraded. They added this undocumented component through an unapproved procedure to mask or to hide the underlying degradation of the product. . . .
>
> You will first hear from Dr. Kevin Hicks, and he is the carbohydrate chemist. He is an expert on Lactulose, and he will tell you that Lactulose is a type of carbohydrate called a disaccharide, and this disaccharide degrades over time. And as time passes, the product breaks down into its component parts. **And you can detect this degradation of the product by testing its pH. And as the product degrades, the pH will decrease**. . . .
>
> In addition, another expert, Dr. John Senior, the gastroenterologist, will tell you . . . that if a product is sufficiently old and the disaccharide has degraded into its component products, the Lactulose simply will not work. The drug will

be ineffective in treating the patient's advanced liver disease.[4]

The government told the Seventh Circuit that it "did not dispute that before being spiked with sodium hydroxide [lots 52-230 and 52-231] were within the pH range, medically effective, and stable." Reply Brief of Appellant at 6. It told the jury that the Defendants injected sodium hydroxide "to mask or hide the underlying degradation of the product." Taking the government's representations at face value, the Seventh Circuit wrote, "In fact, the government did not argue that the Lactulose was unfit, or close to unfit." 175 F.3d at 578. After telling the jury that the lots were "degraded" before the addition of sodium hydroxide, in the next breath government counsel said, "if a product is sufficiently old and the disaccharide has degraded into its component products, the Lactulose simply will not work."

H. The Government Repeatedly Asked Its Lactulose Expert Whether A Decline In pH Indicated That The Product Had Degraded.

Government counsel asked their Lactulose expert, Dr. Kevin Hicks, the following questions:

> "As lactulose degrades, does the pH change? . . . Would the lowering of the pH o[f] the lactulose solution be indicative of degradation? . . . When lactulose is used as a pharmaceutical product is the expiration date reflective at all of the degradation process? . . . Would the addition of sodium hydroxide mask the degradation of the product if you were testing the pH? . . . Is the pH measure a measure-one

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[4] Tr. 12/9/95 at 16, 20-21 (emphases added).

possible measure of the stability of a lactulose product? . . . What would the decrease in pH indicate relating to stability?. . . Would the addition of sodium hydroxide mask any degradation; that is, make it unable to discern degradation?"

Tr. 1582, 1587-89, 1597-1598, 1600-01.

On redirect of Dr. Hicks, government counsel elicited the following testimony:

Q. If you saw a product's pH drop over time from 5.4 to 3.4-and again we are talking about the data points on the stability study 87-227 comparing July '97 to February of '90-what would be the difference in the acidity? What percentage would that be?

A. From 5.4 to 3.2? 5.4 down to 3.2, is that what you are asking?

Q. 5.4 to let's stop at 3.4 for now.

A. To 3.4?

Q. Yes.

A. Again, you have a 100-fold difference.

Q. In a closed container would anything else other than the degradation of the lactulose explain a reduction in pH such as that?

A. Nothing that I am aware of.

> Q. Based on your experience, would you expect to see a reduction in the assay; that is, the percentage of lactulose, whenever you saw such a significant diminution or decrease in pH?
>
> A. There should be a decrease in the assay for lactulose.

Tr. 1652-53 (emphasis added).

Government counsel clearly intended to leave the jury with the impression that when Alra's Lactulose declined in pH to a level of 3.4 or lower, the assay for the active ingredient, or the measure of the product's medical effectiveness, would go down significantly. The post-trial discovery from FDA's files conclusively refuted that argument. That data showed that even when the pH declined below 3.0, the assay for the active ingredient remained unaffected. The government told the Seventh Circuit that "we never argued the material was decomposed due to its aging."

The government also intentionally left the jury with the impression that Lactulose was an unstable product, and that as its pH decreased, there would be a "cascading effect," or a precipitous decline in the product's effectiveness. Government counsel elicited the following testimony from Dr. Hicks:

> Dr. Hicks, are certain chemicals more stable than other chemicals?
>
> A. Certainly, yes.
>
> Q. Is lactulose a fairly stable or a very unfairly stable chemical?

A. Well, compared to other sugars, I would say it's relatively unstable. . . . .

Tr. 1575. Remember, the government told the Seventh Circuit that it never disputed that the Lactulose was "medically effective and stable."

Dr. Hicks went on to testify:

The degradation that you have been describing, is that a gradual or linear degradation or does it accelerate over time?

A. Well, I believe the initial stages would be relatively linear. If we think about the acid catalyzed degradation, what could happen is that since some of the breakdown products are acids themselves, that the pH of the solution or the acidity of the solution-let me just say the acidity of the solution will increase as the degradation occurs. So that could tend to make the degradation rate go faster with time.

Q. Are you familiar with the term "cascading effect."

A. Yes, I have heard that.

Q. Can you describe what that means?

A. Well, as I said, if you have a process that is regulated by the amount of acid, if the amount of acid is increasing in that system, then rather than getting a steady rate, the rate will increase. So there is a cascading or a snowballing type of an effect.

> Q. Would it be fair to say then that as the lactulose begins to degrade it will at first degrade slowly and then the degradation will speed up because there will be the presence of more acids which will cause in effect a snowball effect of a greater degradation?
>
> A. That makes sense in terms of chemical principles, yes.

Tr. 1580.

The government elicited testimony in front of the jury that Lactulose is unstable, that it had an expiration date of 18 months because it degraded over time, that the degradation would increase in a "cascading effect," and that the product would be ineffective in treating seriously ill patients if it was "degraded." The stability data in FDA's files directly contradicted all of these government arguments. After seeing the stability data from other manufacturers, the government turned 180 degrees and said to the Seventh Circuit that it never disputed that the Lactulose was "medically effective and stable," and said, "we never argued the material was decomposed due to its aging." The Seventh Circuit said "the government did not argue that the Lactulose was unfit, or close to unfit." 175 F.3d at 578.

Think about how different Dr. Hicks' testimony should have been if the government's representations to the Seventh Circuit about its trial theory were actually true. According to the government's new theory, Dr. Hicks should have been testifying that Lactulose is a stable drug. Dr. Hicks should have been testifying that Lactulose would not degrade in a

cascading effect. Dr. Hicks should have been testifying that three year-old lots with pH values that had declined by over 100-fold, would still be "medically effective and stable." Dr. Hicks never said that-the government elicited testimony that said just the opposite.[5]

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[5] The government has tried to salvage its trial strategy by claiming that it was arguing that adding sodium hydroxide would increase "degradation" of the product. That is not true; as this motion demonstrates, the government argued all along that lots 52-230 and 52-231 were degraded because of their age, and that Defendants added the sodium hydroxide to "mask" this "degradation." As further proof that the government's case was not based on "degradation" that would occur because of the addition of sodium hydroxide, here is what the government's own expert, Dr. Kevin Hicks, said at trial:

> Q. Thus, could adding sodium hydroxide accelerate, speed up, the degradation of lactulose in those bottles due to those pockets of sodium hydroxide?
>
> A. It's theoretically possible. It would be only localized into the regions where there would be a lot of sodium hydroxide and contact with a small amount of the sugar.
>
> Q. Would there be degradation in the remainder of the solution as well due to the addition of sodium hydroxide?
>
> A. Not if we are talking about just a localized event.

Tr. 11/22/95 at 61.

I. The Government Disputed Defense Expert Testimony That Lactulose Was Stable And That A Decline In pH Would Not Affect The Potency Of the Drug.

The defense called Dr. John F. Robyt, a professor of biochemistry at Iowa State University, as an expert witness. Tr. 4256. Dr. Robyt testified that the bond between the two sugars that form the Lactulose molecule (galactose and fructose) was "very strong." Tr. 4263. As the government is so fond of saying, Dr. Robyt testified that a decline in pH of Lactulose would indicate "degradation" of the active ingredient-he just didn't think that the "degradation" was more than a drop in the bucket. Dr. Robyt prepared a chart, Defendants' Exhibit R-2, which summarized his opinion about "the effect of the drop of pH from 7 to 3 on the amount of Lactulose that would be degraded in a Lactulose syrup." Tr. 4272. Government counsel objected four times to the admissibility of the exhibit. Tr. 4272, 4273, 4274, 4275. Dr. Robyt explained that if Lactulose Syrup was at a pH of 7, and contained 4,000,000 parts of Lactulose, a drop in pH from 7 to 6 would mean that only one part of Lactulose had degraded into one part of acid. "That would leave 3,999,999 parts of Lactulose remaining, and that was based on the composition of the Lactulose syrup and the pH. That would mean that the amount of Lactulose remaining was 99.999 percent." Tr. 4273. Dr. Robyt testified:

> If we go from pH 6 to pH 5, that would mean that there were ten parts of acid produced out of 4 million leaving 3,999,990 parts of Lactulose remaining. That would be 99.9997 percent Lactulose remaining.

> As we drop in pH further, pH 4, there are 100 parts of acid that has been produced out of 4 million parts.
>
> . . .
>
> Between gauge 6 and 3 Lactulose is very stable. It is insignificantly degraded as evidenced by a measurement of pH from 6 to 3 if pH is used as a means of measuring degradation.
>
> The thing about measuring pH is that it's an extremely sensitive method, and it is a change of 100 parts of acid from pH 6 to pH 4 that's for sure. But it's 100 parts of what? 100 parts of a very small number. And so, I say that from 6 to 3, Lactulose is very stable if that's what the pH is.

Tr. 4276-77.

Dr. Robyt also testified that if lots of Lactulose had been stored in bottles for two years, and then tested within specifications, the old lots would be "very, very similar, almost identical" to recently-manufactured lots. Tr. 4278. The stability data in FDA's files proved that Dr. Robyt was right, because it showed that Lactulose is stable as a rock for years, and that declines in pH do not affect the assay for the active ingredient.

According to the government's representations to the Seventh Circuit that the stability data in FDA's files was not material, that the government did not dispute that the old lots of Lactulose were "medically effective and stable," and that "we never argued the material was decomposed due to its aging," the government should have had no cross-examination

for Dr. Robyt. Government counsel should have said, "Dr. Robyt, we agree with everything you say," and sat down.

Instead, government counsel treated Dr. Robyt like the witness he was-a defense expert who was challenging the essence of the government's case. Government counsel challenged Dr. Robyt's qualifications on voir dire, trying to compare his lack of specific expertise on Lactulose with the expertise of the government's expert, Dr. Hicks:

> Q. Dr. Robyt, you indicated that you published approximately 130 articles; is that correct?
>
> A. Yes.
>
> Q. Are any of those articles on the sugar Lactulose? [Dr. Hicks had written articles on Lactulose.]
>
> A. No, they are not.
>
> Q. Have you conducted any laboratory work on the synthesis of Lactulose? [Dr. Hicks had developed a method for synthesizing Lactulose.]
>
> A. No.
>
> Q. Have you conducted any laboratory work on the degradation of Lactulose?
>
> A. No.
>
> Q. Have you conducted any laboratory work on the stability of Lactulose?

A. No.

Q. Have you received any professional awards relating to carbohydrate chemistry specifically Lactulose? [Dr. Hicks had received professional awards for his work on Lactulose.]

A. No.

Q. Have you ever presented papers relating to Lactulose? [Dr. Hicks had presented papers on Lactulose.]

A. No.

[Government counsel]: Your Honor, to the extent that the witness is being offered as an expert on Lactulose disaccharide, that type of sugar, we challenge him.[6]

After challenging Dr. Robyt's qualifications, government counsel asked him a number of questions trying to establish that Lactulose was "less stable" in a diluted liquid form:

Q. So even Lactulose in its pure crystalline form, 100 percent Lactulose, could under some conditions degrade?

---

[6] Tr. 4261-62. Government counsel's strategy worked, of course. The government's expert did have a better resume on Lactulose, and that resume carried the day at trial. That is why the stability data in FDA's files was so essential to the defense. With that data in the courtroom, the government's generalities about a decline in pH indicating "degradation" of Lactulose would have been revealed for the scientific folly they were.

A. Yep.

Q. Is that correct?

A. Yes.

Q. Now, if you take that solid and you put it in with a little bit of water, create a thick solution. The thicker the solution; that is, the less dilute the solution, the more stable it's going to be, correct?

A. Yes.

Q. So in 90 percent solution, that is a solution that contains 90 percent of pure Lactulose and ten percent something else. Let's say, water. It's going to be less stable than the crystalline form but still relatively stable. Would you agree with me?

A. It would be quite stable. It would be less stable. Well-

Q. Just a bit?

A. Just a tiny bit.

Q. And if you add more water, so now we have an 85 percent solution, it's going to be slightly less stable?

A. Yes.

Q. At 80 percent it's going to be slightly less stable, too?

A. Yes.

Q. 75 percent it's going to be slightly less stable still?

A. Yes.

Q. 70, even less stable?

A. Yes.

Q. Okay. Incrementally, 65 percent, it's going to be less stable?

A. Yes.

Q. 60 percent, less stable still?

A. You want to keep this up, sure. Yes.

Q. We will stop at some point, I assure you. 55 percent?

A. Yes.

Q. Let's talk about approximately a 50 percent solution?

A. Yes.

Q. Let's say you have lactulose that's mixed with approximately 50 percent of something else. You have a little bit of a breakdown of

> degrading products, and you have got some water. That's not going to be as stable as pure Lactulose, is it?
>
> A. No, but-

Tr. 4293-94. The Government told the Seventh Circuit that it did not dispute these lots were stable. Why was government counsel asking questions to establish that the lots were not stable?

Government counsel then used a certificate of analysis from the manufacturer that supplied Alra's lactulose concentrate, and pointed out that the raw material was approximately 50% water, and that it contained other sugars, such as lactose and galactose. Government counsel suggested that the presence of those other sugars could be by-products of degradation in the Lactulose that had already occurred. Tr. 4296-4302.

Government counsel also challenged Dr. Robyt's opinion that Lactulose would not degrade in a "cascading effect" when its pH approached 3:

> So the percentage of the Lactulose disaccharide over time will decrease, not linearly, but exponentially?
>
> A. If you have a cascading effect, yes.
>
> Q. And does Lactulose degrade in an acidic condition in a cascading effect?
>
> A. I don't think so.
>
> Q. Have you read any literature on that?

A. No.

Q. What's the basis of your opinion?

A. Well, a pH of 3, the amount of acid is very low and, therefore, I don't-I think you would still be in this part of the curve. And I don't know what happens when you get down to pH of 1 or 0. Indeed, that could be if you got to pH 1 or 0. It will go to 0. . . .

Q. Sir, you don't know that's what occurs at pH of 3, do you?

Tr. 4322.

During cross-examination of Dr. Robyt, government counsel also emphasized the government's theory of the case:

Q. Sir, would the increase of sodium hydroxide in any way reverse the degradation that we've been discussing? Put the Lactulose molecule back together again?

A. No.

Q. Would the decrease-the injection of sodium hydroxide in any way mask the degradation if I am measuring degradation by measuring pH?

A. Yes, of course.

Tr. 4331.

J. The Government Called A Gastroenterologist To Testify That "Degraded" Lactulose Could Kill Seriously Ill Patients.

After calling Dr. Hicks to testify that a decline in pH indicated that Lactulose had "degraded," the Government called Dr. John Senior, a gastroenterologist, to testify about the effect of "degraded" Lactulose. As this Court stated at a post-trial hearing on September 11, 1996:

> [o]ne of the most impressive witnesses at the trial, if not the most impressive witness, was the Government's expert, Dr. Senior. On page 27 of the transcript of his testimony, he is asked, I believe, by [Government counsel]: "Question: if Lactulose is degraded into monosaccharide components, would it work to treat portal systemic encephalopathy. Answer: No, it won't work if it is degraded or split because the split products of Lactulose are fructose and galactose which are easily absorbed sugars. They are gone. They never get to the colon." And he goes on in more detail on the following page, to talk about how if the Lactulose is degraded, it won't be medically effective. Then he is asked at line 17 of page 28: "Question: And would a physician be able to ascertain what was wrong if Lactulose had broken down into disaccharide forms?" Now, there would be absolutely no purpose in asking that question, it seems to me, unless the Government was contending that the question was relevant to the fact situation before the jury. The question addresses a situation where Lactulose had broken down into its [monosaccharide] form. And Dr. Senior, in what was, in my distinct recollection, an

> absolutely devastating answer said the following: "That makes it very hard on the physician because a lot is going on in these sick patients. They have got a failing liver. They often have. They are now getting failure of the brain function. They often have kidney failures that goes with the liver failures. They have got a lot of problems, and the last thing a physician is going to think of when he prescribes a drug is that it isn't what it is supposed to be." . . .
>
> Small wonder that the Court has a serious concern that, due to the tactics of the Government, the jury gained the impression that this Lactulose was dangerous to any patient who used it.

Motions hearing, 9/11/96 at 10-11 (emphasis added).

K. During Argument On Defendants' Rule 29 Motions, The Government Argued That The Lots Were "Decomposed To The Degree That [They] Could No Longer Be Used As A Medicine."

On January 24, 1996, during oral argument on Defendants' Rule 29 motion, government counsel told this Court that "[t]he easiest indicator of deterioration is the reduction in the pH . . . ." Tr. 1/24/96 at 125. Government counsel told the Court that "the sodium hydroxide addition . . . would mask the degradation." Tr. 1/24/96 at 126. Government counsel told the Court, "what Dr. Hicks testified to that the product was decomposing-the testimony of Dr. Hicks was that that was evidence that the drop in pH was evidence of the decomposition, and that, with regard to the expiration date, the government's theory as was added to mask that." Tr. 1/24/96

at 148. Government counsel told this Court during Rule 29 argument, "as Dr. Hicks testified, the product will degrade over time, and after 18 months the product would have degraded to such a point that it would not longer be appropriate for use as a medicine . . . ." Tr. 1/24/96 at 149.

During Rule 29 argument, this Court said, "Well, what we are talking about here is a problem with tense, I think. Count 3, just, for example, talks about something [the alleged addition of sodium hydroxide] that was done on or about August 12, 1988. And it talks about a decomposed substance as of that date. You are talking about something that may have happened in the future after August 12th." Government counsel responded, "No, your Honor. As of August 12th, 1988, when they were packaging this product for resale, we had a product that had been manufactured in, I believe it was either December of 1985 or January of 1986. That is when the raw material had been manufactured; that that material, according to the testimony of Dr. Hicks, would begin to decompose as of its time of manufacture and it's either December of '85 or January of '86; that the expiration date based on the testing that had been done and the literature was that Lactulose by 18 months after its manufacture would be decomposed to the degree that it could no longer be used as a medicine." Tr. 1/24/96 at 150 (emphasis added).

L. The Government Attacked The Testimony Of A Chemist Who Tested Alra's Reserve Samples Of Lactulose And Found Them All Within Specification For Potency Years After Manufacture, And Even Though The pH Of The Lots Had Declined.

At trial, the defense called Dr. Sneh Bhandari, a Ph.D chemist, who tested retained samples of Lactulose lots 52-230 and 52-231, and samples from other Alra lots, during the trial.

Although lots 52-230 and 52-231 were ten years old, and their pH values had dropped below 3, both lots tested above 100% for label claim of Lactulose content. Tr. 2/5/96 at 3-8.

According to the government's representations to the Seventh Circuit, this testimony should have been non-controversial, since the government now claims that it "did not dispute" that the lots were "medically effective and stable." Government counsel did not treat the testimony as non-controversial. Instead, government counsel repeated the theory that a decline in pH was evidence of "degradation." "And the degradation of the product with organic acids as a by-product could explain that increase in acid formation which corresponds to a decrease in pH; is that right?" Tr. 2/5/96 at 16. Government counsel challenged Dr. Bhandari's expertise- "Your laboratory typically does food and vitamin testing; isn't that right? . . . You don't do much Lactulose testing or drug testing; isn't that right?" Tr. 2/5/96 at 17.

Finally, government counsel suggested to the jury that Defendants had tampered with the samples: "you have no idea what's happened to these bottles between 1988 and 1996, particularly January 30th of 1996, do you?" Tr. 2/5/96 at 18.

M. The Defendants Testified That They Had No Reason To Increase The pH Of The Lactulose, And The Government Attacked Their Credibility

Defendant Neelam Bhutani testified in her own defense. She said that in early August, 1988, her laboratory tested lots 52-230 and 52-231. Government Exhibit 100 showed that Alra tested two samples from lot 52-230, and got pH results of 5.3 and 5.4. Government Exhibit 101 showed that Alra tested two samples from lot 52-231, and got pH results of 5.6 and 5.3. Tr. 1/30/96 at 84-87. On direct, her counsel asked, "Based on that

information, can you think of any reason why the pH of these lots would then be adjusted within a week after the testing?" She answered, "No, I can't think of any reason." Tr. 1/30/96 at 87. Mrs. Bhutani denied having any knowledge that Alra employees had injected any substance into lots 52-230 and 52-231. Tr. 1/30/96 at 87-88.

During cross, government counsel asked Mrs. Bhutani to confirm that she knew FDA had set an 18-month expiration date on Alra's Lactulose. Tr. 1/31/96 at 159-60. Government counsel cross-examined Mrs. Bhutani at length about the age of the raw material that had gone into lots 52-230 and 52-231:

> Q. Will you agree with me then that the [raw material of the Lactulose] product would have to have been manufactured some time before January 14th of 1986?
>
> A. Yes.
>
> Q. So as of the time these two lots were released in August of 1988, this material had existed throughout 1986, 1987, and seven months of 1988, correct?
>
> A. Yes.
>
> Q. And in addition, it was given an expiration date until September of 1989?
>
> A. Yes.
>
> Q. Correct? So at this point in time, depending on when this product was actually made, by the time the product, 52-230 and 52-231, reached its expiration date of September 1989, is it not

accurate that the raw material had been manufactured at least 45 months earlier?

A. Probably.

Q. Well, is there any doubt in your mind?

A. '89 to '86-maybe 42. Yes, if the math is right, I am not going to-

Q. Now, at this point in time, the time that you released the product, August of 1988-

A. Yes.

Q. -the position of the FDA was that Alra had submitted data, had data that would support an expiration date of up to 18 months, correct?

A. I have no knowledge of what was submitted to FDA. What I had with me, I can testify to that because I did not deal with FDA at all.

Q. Okay. But you wrote to Searle telling them that it was 18 months from the date of manufacture of the raw material, correct?

A. Yes.

Q. And is it not true that Alra, throughout this time period, 1989, 1990, 1991, 1992, was requesting an extension in the expiration date from 18 to 24 months on its Lactulose?

A. Yes.

Q. And isn't it true that the FDA was denying this request?

A. I told you I am not involved in dealing with FDA. I was not. I don't know what they were doing, denying or they were requesting or what they were doing. I had no knowledge of those dealings.

Q. At the time the product was released in August of 1988, the time you signed off on it-

A. Yes.

Q. -you had no data whatsoever with regard to the stability of Lactulose for a period beyond the then current age of this product, did you?

A. We had 40 degree stability data on one of the lots for six months and -

Q. You had 40 degree stability data on ne of the lots in 1989, ma'am?

Tr. 1/31/96 at 165-67.

At trial, the government attacked Mrs. Bhutani's credibility, suggesting in repeated questioning that she knew, or should have known, that the product was not stable when it was released. Think about how different that cross would have been if government counsel had said, "Mrs. Bhutani, you were right, that product was 'medically effective and stable.' But then you added sodium hydroxide bottle-by-bottle (for no reason that we discern) and that made the product dangerous, right?"

Dr. Raj Bhutani testified in his own defense. He testified that when he got the lab results on lots 52-230 and 52-231, there was no reason to doctor or fix the batches in any way: "It had almost hundred percent of its potency. It was--microbiologically, it was pure. pH was in good range. Physical inspection was pretty good. No, there was no reason whatsoever." Tr. 1/31/96 at 22-23. Dr. Bhutani also testified that based on his experience with Lactulose, and based on stressed stability testing Alra had done at high temperatures, he believed the lots were stable, even though they had been manufactured in 1986. Tr. 1/31/96 at 26-27. Dr. Bhutani testified that "There was absolutely no reason" for him to instruct his employees to inject sodium hydroxide into lots 52-230 and 52-231. Tr. 1/31/96 at 27.

Government counsel cross-examined Dr. Bhutani about the defense assertion that the Lactulose was stable even though it was several years old. Dr. Bhutani relied on stability tests Alra had performed on several research and development batches of Lactulose. Government counsel asked repeated questions about the size of Alra's research and development batches of Lactulose, which were generally two liters in size. Tr. 2/5/96 at 185-88. Government counsel specifically asked, "Other than making these small batches of under a gallon, what other research and development work did you do with regard to Lactulose prior to the time that you made lots 52-230 and 52-231?" Tr. 2/5/96 at 187.

N. During Closing Argument, Government Counsel Argued That Lots 52-230 And 52-231 Were "Degraded," That Defendants Added Sodium Hydroxide To "Mask" That "Degradation," And That "Degraded" Lactulose Might Kill Seriously Ill Patients.

In closing argument, Government counsel repeated the argument that a decline in pH meant that the Lactulose had degraded, and that the "degraded" Lactulose sold by the Defendants may have killed patients:

> Now, after you heard about all the chemistry, you heard from a physician, and that was Dr. John Senior. **And he told you the medical consequences of this degradation and why in very human terms this all matters.** . . .
>
> But as Dr. Senior pointed out, the Lactulose has to reach the large intestine in order for it to work. If the Lactulose is already broken down, **if it is already degraded** into its monosaccharide form, the monosaccharides will be absorbed in the small intestine, they'll be digested and the Lactulose in its disaccharide form will never reach the colon, the site of the effective treatment. And it will be rendered ineffective in treating patients with hepatic coma or portal systemic encephalopathy.

Memorandum Opinion of the Honorable John F. Grady, December 17, 1997, quoting Government's first closing argument (emphases added).

Both Government counsel also argued that the motive for adding sodium hydroxide to lots 52-230 and 52-231 was to mask the "degradation" of those lots:

> They did this to make sure that if anyone tested the pH of the drug product, it would test high. They wouldn't know it was old, they wouldn't know it had degraded. They did this so the consumers couldn't know of the truth about the products that they were buying. They wouldn't know the pH had dropped, they couldn't tell the product had degraded, and they wouldn't suspect that it had passed the expiration date.

Tr. 5585 (first closing).

> They raised the sodium hydroxide, so if three months or six months down the road AARP or - I forgot the other company they sold this to - Bioline I think it was, checked the pH, it would appear that this stuff was new. It didn't just have to be within spec, it had to be new because this stuff was labeled with a September of 1989 expiration date.

Tr. 5805 (rebuttal closing).

Think about how different the closing arguments would have been if government counsel had told the jury, "They injected a chemical into lots that were 'within the approved pH range, medically effective, and stable.'" Government's Reply Brief at 6. If the jury had heard an

argument like that, would it have found that the Defendants had a motive to add the sodium hydroxide?[7]

O. In Post-Trial Submissions To The Probation Department, The Government Argued That A Decline In pH Evidenced "Degradation."

In its April 22, 1996 submissions to the Probation Officer, the government wrote: "If the lactulose degrades and fails to reach the colon in its original form, it is rendered ineffective . . . . The degradation of the product is evidenced by a decrease in the pH . . . ." April 22, 1996, letter re Neelam Bhutani to Ms. Elisa J. Ehrlich, at 7.

P. The Government's Opposition To Post-Trial Discovery Restated The Government's Theory Of Motive.

After the government submitted its Version of the Offense to the Probation Department in 1996, the United States Pharmacopeia ("USP") proposed a downward revision of the acceptable pH range for Lactulose, from 3.0 - 7.0 to 2.5 - 6.5. The USP proposal stated:

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[7] To the extent that the Seventh Circuit relied on the government's theory that ALRA had placed "inaccurate expiration date[s]" on the Lactulose lots, the Government's first witness, Dr. Eric Duffy, a Ph.D review chemist employed by FDA, conceded that one of several reasonable interpretations of Dr. Bhutani's correspondence with the FDA was that Alra was allowed to sell "old" lots of Lactulose it had on hand based on passing final lab testing of the product. Tr. 333-35. The jury acquitted defendants on counts 2 and 5, which alleged that the Lactulose lots had been labeled with inaccurate expiration dates.

> [b]ased on information received that stability data has shown a downward trend in pH over time, it is proposed to revise the pH range in this monograph. The proposed pH change is reported not to have any significant impact on the safety and quality of this product: it does not in any way affect the laxative properties of the product, and it does not affect the level of the related substances.

J.A. 284-85.

Defendants moved for a new trial and for discovery of Lactulose stability data in FDA's files consistent with the USP proposal. The district court ordered discovery. The government opposed the motion for trial, arguing, among other things, that the defense should have subpoenaed stability data because the government had notified the defense of its theories concerning the relevance of pH data on Lactulose. The government's opposition argued that declining pH values in Alra's stability data

> was thus relevant to establish Defendants' motive in injecting sodium hydroxide into the old Lactulose before releasing it on the market. The declining pH indicated the Lactulose was degrading and would be past its expiration date, so the Defendants ordered the injection of a base (sodium hydroxide) to mask the fact that the product was old and had passed its expiration date.

Government's Opposition to Defendants' Post-Trial Motion for a New Trial Based on Newly Discovered Lactulose Stability Evidence, served June 12, 1997, at 14 & n.8 (emphasis added). How does the statement that the "declining pH indicated the

Lactulose was degrading and would be past its expiration date" square with the representation to the Seventh Circuit that the government "did not dispute" that the Lactulose was "medically effective and stable" before the alleged addition of sodium hydroxide? How does the statement that "the product was old and had passed its expiration date" square with the representation that "we never argued the material was decomposed due to its aging?"

III. A COMPARISON OF THE GOVERNMENT'S "VERSION OF THE OFFENSE" BEFORE AND AFTER TRIAL DRAMATICALLY ILLUSTRATES THE GOVERNMENT'S CHANGE OF POSITION.

In 1996, before the district court ordered discovery of the stability data in FDA's files, the government had submitted a "Government's Version of the Offense" to the Probation Department. The government recently submitted a Sentencing Memorandum to the district court in preparation for a sentencing hearing scheduled for January 11, 2000. Government counsel edited the 1996 version of the "Government's Version of the Offense" in a telling way.

The 1996 version contained the following paragraph:

> Because Lactulose degrades, it loses its therapeutic efficacy over time. The degradation of the product is evidenced by a decrease in the pH (or rise in acidity) of the finished product. If sodium hydroxide (a base) is added to Lactulose, the pH will rise, but the degradation will not be reversed. Accordingly, injecting sodium hydroxide into finished bottles of Lactulose will simply serve to mask the degradation of the product.

Note how this 1996 "Government's Version of the Offense" contradicts the representations made to the Seventh Circuit. This 1996 version does not say that the Lactulose was "medically effective and stable" before the addition of sodium hydroxide; it says that the addition of sodium hydroxide "will simply serve to mask the degradation of the product."

For the 1999 "Government's Version of the Offense," counsel edited that paragraph to read:

> Because Lactulose, like all other chemicals, degrades, it will necessarily lose its therapeutic efficacy over time. The only way to know the rate at which any particular formulation of Lactulose Syrup, U.S.P., will degrade, and thereby to know for how long it will retain its therapeutic effectiveness, would be to test it over time.

What happened to "masking the degradation?"

CONCLUSION

Defendants respectfully request that the Department of Justice re-examine its conduct in this case, and confess error in response to the Petition for Certiorari currently pending before the Supreme Court.

Very truly yours,

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January 11, 2000

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Re: United States v. Bhutani, et al.

Dear Counsel:

Thank you for your courtesy and patience yesterday. I realize that because I got emotional and frustrated, I was less articulate, and less polite, than I would like to be. I remain convinced that the Department of Justice has a fundamental misunderstanding of what happened in this case. I hope that the letter I left with you yesterday shows you why I feel so strongly. I am writing this second letter as an additional attempt at persuasion.

During the meeting with Doug, Larry, and Bob yesterday, Bob recalled that a jury instruction had made reference to "degradation." Bob suggested that this jury instruction showed that the government had not contended

that Lactulose lots 52-230 and 52-231 were unstable or ineffective prior to the alleged addition of sodium hydroxide. The jury instruction that Bob was remembering defined "decomposed substances," not "degradation," and conclusively demonstrates that the government contended that lots 52-230 and 52-231 were medically ineffective prior to the alleged addition of sodium hydroxide. The Indictment and the government's requested jury instructions show that the government presented a theory of conviction that lots 52-230 and 52-231 were "adulterated" because they were composed of a "decomposed substance." The government agreed to a jury instruction that a "decomposed substance" meant that "the Lactulose active ingredient had decomposed so that it no longer met applicable testing specifications . . . ."

Overt Act 2 in the conspiracy count alleged: "BALDEV RAJ BHUTANI and NEELAM BHUTANI directed ALRA employees to add an undocumented substance, namely additional amounts of Sodium Hydroxide (NaOH), to partially decomposed Lactulose in the finished generic drug product Lactulose Syrup, USP . . . ." (Emphasis added).

Count 3 of the Indictment alleged that lot 52-230 was adulterated on August 12, 1998 in three separate ways: "(1) this drug product consisted in part of a decomposed substance, namely decomposed lactulose raw material; (2) the drug product had not been manufactured in accordance with Good Manufacturing Practice; and (3) the defendants materially altered the manufacturing procedures for this drug product by adding an undocumented substance, Sodium Hydroxide . . . ."

It is clear from Overt Act 2 and the date of adulteration in Count 3 (the date of the alleged rework), that the government contended that the product consisted of a "decomposed substance" prior to the alleged addition of sodium hydroxide. Government's Requested Jury Instruction No. 44 read:

DEFINITION OF "ADULTERATION"
(IN CONTEXT OF COUNT THREE)

. . .

You may find that this particular lot of Lactulose was "adulterated" in one of three ways.

First, Count Three alleges that Lactulose lot 52-230-P was adulterated in that this drug product consisted in part of a decomposed substance, namely decomposed Lactulose raw material. If you unanimously find this to be the case, you should find this lot of Lactulose "adulterated."

Second, Count Three alleges that Lactulose lot 52-230-P was adulterated in that the defendants materially altered the manufacturing procedures for this drug product by adding an undocumented substance, Sodium Hydroxide, more than two years after the original manufacture of this drug product. If you unanimously find this to be the case, you should find this lot of Lactulose "adulterated."

Third, Count Three alleges that Lactulose lot 52-230-P was adulterated in that the drug product had not been manufactured in accordance with Good Manufacturing Practices. . . .

Judge Grady read this instruction to the jury. Tr. 5840-41.

The government agreed to a modified version of Alra Requested Instruction No. 4, which provided:

> In Counts Three, Six, Seven, and Eight, the government alleges that certain raw material or finished product lots of Lactulose were "decomposed." For purposes of these counts, "decomposed" means more than that the Lactulose active ingredient had begun to degrade; all drug products begin a degradation process to a greater or lesser degree after manufacture. The government must prove beyond a reasonable doubt that at or about the time alleged in the particular count the Lactulose active ingredient had decomposed so that it no longer met applicable testing specifications in order for you to find that the Lactulose lots specified in Counts Three, Six, Seven, and Eight were "decomposed."

(Emphasis added). Judge Grady read this instruction to the jury. Tr. 5842.

Following the government's proposed jury instructions, the jury may have voted to convict on Count 1, the conspiracy, based on Overt Act 2, which alleged that Defendants added sodium hydroxide to a "decomposed substance," defined as "decomposed so that it no longer met applicable testing specifications." The jury may have voted to convict on Count 3 based on the government's theory that lot 52-230 was adulterated because it "consisted in part of a decomposed substance," defined as "decomposed so that it no longer met applicable testing specifications."

The government's theories of conviction on Counts 1 and 3 alone conclusively demonstrate that the government contended the lots were not medically effective and stable. The representations to the Seventh Circuit that the government "did not dispute that before being spiked with sodium hydroxide [lots 52-230 and 52-231] were within the pH range,

medically effective, and stable," and "we never argued the material was decomposed due to its aging" were thus clearly wrong. So was the Seventh Circuit's opinion, parroting the representations of the government, that "the government did not argue that the Lactulose was unfit, or close to unfit." 175 F.3d at 578.

The government told the Seventh Circuit that it never disputed that the lots were "stable." Government counsel told the jury something different in closing argument: "Dr. Hicks explained how Lactulose is an unstable sugar. It breaks down easily. And what that basically means, it degrades." Smolover closing at 36.

Government counsel's Rule 29 argument to the district court also directly contradicted the representations to the Seventh Circuit that the government "did not dispute that before being spiked with sodium hydroxide [lots 52-230 and 52-231] were within the pH range, medically effective, and stable," and "we never argued the material was decomposed due to its aging." Government counsel told the district court during Rule 29 argument, "as Dr. Hicks testified, the product will degrade over time, and after 18 months the product would have degraded to such a point that it would not longer be appropriate for use as a medicine .... Lactulose by 18 months after its manufacture would be decomposed to the degree that it could no longer be used as a medicine." Tr. 1/24/96 at 149-50.

Bob suggested that because this Rule 29 argument did not occur in front of the jury, the representations to the Seventh Circuit were still accurate. That position is untenable. You did not qualify the representations to the Seventh Circuit by saying that government counsel presented one theory to the district court, but a different theory to the jury. Even more important, government counsel's Rule 29 arguments illustrate government counsel's understanding, during the trial, of what the government's arguments to the jury meant. We have

argued that in the context of the trial, the government's use of the word "degradation" conveyed a very clear impression to the jury that the product was ineffective and unstable. Ask anyone what a "degraded" or "expired" product is, and I doubt if you would hear anyone say it means a product that is "medically effective and stable." References to "degradation" as a continuous process do not mean that references to "degraded" or "expired" product would be understood by a jury of laypersons to mean "medically effective and stable." If you simply read the quotations in Judge Grady's opinion, and substitute the phrase "old, but medically effective and stable" every time government counsel used the word "degraded," "degradation," or "expired," you will see that the meaning and emphasis and jury appeal of the government's arguments would be quite different. It's not sexy to argue to a jury that the lots were "medically effective and stable," and that the government wants to put people in jail for not honoring an expiration date that did not affect the quality of the product.

At the meeting, you seemed to contend that the government's trial theory was that a decline in pH evidenced "degradation" that had no correlation to the medical effectiveness, and that all of the government's references to "degradation" simply referred to the aging of a product that had passed its expiration date. Why didn't the government tell the jury that? If that was my theory, I would argue to the jury that "a decline in pH reflects that the product was aging, even though the pH may not correlate to the medical effectiveness of the product. To mask the age of the product, the defendants added sodium hydroxide to raise the pH." Instead, government counsel told the jury:

> The defendants instructed their employees to open up the bottles of Lactulose, those 1986 bottles, and inject a chemical called sodium hydroxide into the bottles in order to raise the pH and make it appear that the

product had not, in fact, degraded. They added this undocumented component through an unapproved procedure to mask or to hide the underlying degradation of the product. . . .

You will first hear from Dr. Kevin Hicks, and he is the carbohydrate chemist. He is an expert on Lactulose, and he will tell you that Lactulose is a type of carbohydrate called a disaccharide, and this disaccharide degrades over time. And as time passes, the product breaks down into its component parts. **And you can detect this degradation of the product by testing its pH. And as the product degrades, the pH will decrease. . . .**

In addition, another expert, Dr. John Senior, the gastroenterologist, will tell you . . . that if a product is sufficiently old and the disaccharide has degraded into its component products, the Lactulose simply will not work. The drug will be ineffective in treating the patient's advanced liver disease.[1]

. . .

Now, after you heard about all the chemistry, you heard from a physician, and that was Dr. John Senior. **And he told you the medical consequences of this degradation and why in very human terms this all matters. . . .**

But as Dr. Senior pointed out, the Lactulose has to reach the large intestine in order for it to work. If the Lactulose is already broken down, if it is already degraded into its monosaccharide form, the monosaccharides

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[1] Tr. 12/9/95 at 16, 20-21 (emphases added).

> will be absorbed in the small intestine, they'll be digested and the Lactulose in its disaccharide form will never reach the colon, the site of the effective treatment. And it will be rendered ineffective in treating patients with hepatic coma or portal systemic encephalopathy.

Smolover closing at 40-41 (emphases added).

You can't tell a jury that "degraded" Lactulose will kill patients, tell the jury that Alra's Lactulose was "degraded," and then tell the Seventh Circuit that the government "did not dispute that before being spiked with sodium hydroxide [lots 52-230 and 52-231] were within the pH range, medically effective, and stable," and "we never argued the material was decomposed due to its aging."

The government repeatedly contended that Judge Grady had not reviewed the record carefully, and had an incorrect memory of the government's trial arguments. To the contrary, Judge Grady carefully considered the government's arguments and the trial record. Judge Grady was far more articulate than I was about the context in which the government used the word "degradation." At a post-trial hearing on September 11, 1996, Judge Grady said:

> The government denies that it ever said or implied that the degree of degradation reached by the two lots in question presented a danger to the user.

I have a very substantial question in my mind as to whether the government's position is supported by the record. First of all, there is the common sense proposition that degradation that has not reached the dangerous level and, in fact, is remote from a dangerous level would not be the subject of the constant repetition it received during this trial.

In Miss Smolover's opening statement, I don't know how many times-and I don't have the whole opening statement; I just have an excerpt from it-I don't know how many times she mentioned the word or used the word "degradation" or "degrade." And it is at the moment impossible for me to read that opening statement without concluding that she was saying that this was a dangerous situation because the Lactulose had degraded and that the defendants attempted to mask that degradation by changing the pH, the only index that someone would have, to determine whether, in fact, there had been degradation.

There is a particular reference at page 16 of the transcript where Miss Smolover said the following in her opening statement to the jury, beginning at line 7:

"That is not all they did. Before they shipped the product our the door, they took another important step to cover up the fact that they were shipping expired product. Oftentimes large buyers or wholesalers of generic drug products will test a product once it has been received and they will test a product like Lactulose for something like pH or acidity,

and those tests are designed to assure that the product is not degrading, that it is still within specification."

Now, I emphasize the phrase, "still within specification." Miss Smolover is saying that the test for pH would determine whether the product was still within specification, and specification would be 3 to 7.

She goes on to say:

"Baldev Raj Bhutani and Neelam Bhutani knew this. In fact, Alra was selling these products to large pharmaceutical wholesalers including the AARP and Biolab. So what did the Bhutanis do? The defendants instructed their employees to open up the bottles of Lactulose," and so on.

The next paragraph:

"They added this undocumented component through an unapproved procedure to mask or hide the underlying degradation of the product."

Now, it is difficult for me to read that language without having the impression that degradation and falling below specifications are one and the same and that the purpose of the addition of the pH was to mask the fact that the product fell below specification.

One of the most impressive witnesses at the trial, if not the most impressive witness, was the Government's expert, Dr. Senior. On page 27 of the transcript of his testimony, he is asked, I believe, by Miss Smolover:

"Q if Lactulose is degraded into monosaccharide components, would it work to treat portal systemic encephalopathy?

"A No, it won't work if it is degraded or split because the split products of Lactulose are fructose and galactose which are easily absorbed sugars. They are gone. They never get to the colon."

And he goes on in more detail on the following page, to talk about how if the Lactulose is degraded, it won't be medically effective. Then he is asked at line 17 of page 28:

"Q And would a physician be able to ascertain what was wrong if Lactulose had broken down into disaccharide forms?"

Now, there would be absolutely no purpose in asking that question, it seems to me, unless the Government was contending that the question was relevant to the fact situation before the jury. The question addresses a situation where Lactulose had broken down into its [monosaccharide] form.

And Dr. Senior, in what was, in my distinct recollection, an absolutely devastating answer said the following:

"That makes it very hard on the physician because a lot is going on in these sick patients. They have got a failing liver. They often have. They are now getting failure of the brain function. They often have kidney failures that goes with the liver failures. They have got a lot of problems, and the last thing a physician is going to think of when he prescribes a drug is that it isn't what it is supposed to be."

Now, the government knew what the answer was going to be, and the answer was either relevant to the case before the jury or it wasn't. And if we weren't dealing with a situation where, unbeknownst to the physician and the patient, the Lactulose wasn't going to get through to the colon, that answer should not have been elicited from that witness.

Small wonder that the Court has a serious concern that, due to the tactics of the Government, the jury gained the impression that this Lactulose was dangerous to any patient who used it.

Now, turning to Miss Smolover's closing argument, and referring to page 40 of the transcript, at line 6:

"Now, after you heard about all the chemistry, you heard from a physician, and that was Dr. John Senior, and he told you the medical consequences of this degradation and why, in very human terms, this all matters."

What does the phrase "this degradation" refer to? Well, the immediately

> preceding paragraph referred to the very Lactulose involved in the two lots in this case where Miss Smolover said:
>
> "The chemical is injected to hide the declining pH. It didn't make the product whole again"-note the verb "didn't," referring to the very events in this case-"it didn't make the product whole again; it didn't reverse the degradation. In fact, it sped it up."
>
> And then immediately following we have the reference to the testimony of Dr. Senior concerning the medical consequences of this degradation. . . .

Motions hearing, 9/11/96 at 8-12 (emphasis added).

I am also unsure of Bob's understanding of what "stable" means. The government contended throughout the trial that lots 52-230 and 52-231 should not have been sold because they were already inappropriate for use as medicine, and because there was no data to establish that the lots would remain potent through the expiration period stamped on the bottles. The defense argued that Lactulose was stable as a rock, and that the lots would remain effective for years after the expiration date stamped on the bottles. The stability data in FDA's files demonstrated that the defense was right. That's why Judge Grady thought the stability data was helpful to the defense and material. I got the impression from our meeting that Bob thinks "stable" means within specifications today, even if it may go out of specification tomorrow. That is not what any participant at trial would understand the word "stable" to mean. As the jury was told repeatedly by FDA witnesses, "stability" studies are tests designed to ensure the potency of the product throughout its shelf life, not just on the date of its release. The Seventh Circuit understood the

government's representations to mean that "the government did not argue that the Lactulose was unfit, or close to unfit." 175 F.3d at 578 (emphasis added).

Government counsel did not tell the jury that Lactulose was "stable." They said just the opposite. In addition to saying, "Lactulose is an unstable sugar. It breaks down easily,"[2] Deborah told the jury in closing argument:

> And it's because lactulose degrades, it's because Lactulose does not remain stable over time, that it's given an expiration period by the FDA.
>
> Now, Dr. Hicks further explained that this degradation process is not linear. It accelerates, cascades or snowballs, and that that happens all the time. It begins happening the moment that the Lactulose is synthesized into a liquid, into that concentrate syrup in those drums. And it continues to degrade once it's formulated into its finished product form. Even when it is within USP specifications, even when it's in the specifications of pH 3 to 7, it's constantly degrading into its component parts, and that degradation speeds up.
>
> And most importantly what Dr. Hicks told you is that degradation process cannot be reversed. It can't be stopped. But it can be hidden. The truth can be masked. And Dr. Hicks told you how the truth can be masked.
>
> He explained the effect of adding the base sodium hydroxide to individual bottles of

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[2] Smolover closing at 36.

> Lactulose. He told you of the very important scientific fact that sodium hydroxide, a base, will raise the pH in those bottles and mask the evidence that the product has degraded. It will not put the Lactulose molecules back together, again, but it will hide the fact that they've come apart.

Smolover closing at 37-38. Is that a description of a "medically effective and stable" product? Is that a description of a product that the government "never argued . . . was decomposed due to its aging?"

The government alleged that lots 52-230 and 52-231 consisted of decomposed substances before the alleged rework, and agreed with a jury instruction that a decomposed substance meant that the active ingredient was "decomposed so that it no longer met applicable testing specifications . . . ." Tr. 5842. The government told the district court, "as Dr. Hicks testified, the product will degrade over time, and after 18 months the product would have degraded to such a point that it would not longer be appropriate for use as a medicine . . . . Lactulose by 18 months after its manufacture would be decomposed to the degree that it could no longer be used as a medicine." Tr. 1/24/96 at 149-50 (emphasis added). Government counsel told the jury, "Lactulose is an unstable sugar. It breaks down easily. And what that basically means, it degrades." The government told the jury over and over again that the lots were "degraded" and "expired," and called a gastroenterologist to say that "degraded" Lactulose might kill seriously ill patients. The government told the Seventh Circuit that it "did not dispute that before being spiked with sodium hydroxide [lots 52-230 and 52-231] were within the pH range, medically effective, and stable," and "we never argued the material was decomposed due to its aging."

The words "degraded," "decomposition," and

"expired" have well-understood meanings. They do not mean "medically effective and stable." They do not mean different things on different days to different audiences.

My clients are counting on you to do the right thing. We would appreciate a response to my letters by Monday, January 17.

Very truly yours,

Christopher B. Mead